

Nitrite Photolysis in the Presence of Oxygen. An Improved Synthesis of 32-Oxygenated Lanostanes

By John Allen, Robin B. Boar,* and James F. McGhie, Chelsea College, London SW3 6XL
Derek H. R. Barton, Imperial College, London SW7 2AY

Photolysis of 3 β -acetoxy-5 α -lanostan-7 α -yl nitrite in the presence of oxygen affords 3 β -acetoxy-7 α -hydroxy-5 α -lanostan-32-yl nitrate. The implications to synthesis of this modified procedure are outlined and are exemplified by the synthesis of the 32-alcohol (I; R¹ = Ac, R² = H) and the 32-aldehyde (II; R = Ac).

WE have previously described the synthesis of 32-functionalised lanostanes *via* the photolysis of 7 α -nitrite esters.¹ Biosynthetically the 32-alcohol (I; R¹ = R² = H) and the 32-aldehyde (II; R = H) are of particular importance.² We now report a more direct route to the latter compounds involving a modified nitrite photolysis procedure.

Oxygen was slowly bubbled through a benzene solution of the 7 α -nitrite (III; R = NO, X = H) during irradiation with a high pressure mercury arc lamp. The previously observed¹ (nitrogen atmosphere) 7 α -hydroxy-

32-oxime (IV) was not formed, but on chromatography a new less polar product was isolated in 44% yield. Analytical and spectroscopic data (see Experimental section) indicated that this compound was 3 β -acetoxy-7 α -hydroxy-5 α -lanostan-32-yl nitrate (III; R = H, X = ONO₂). A plausible mechanism for this transformation is shown in the Scheme. There are precedents both for capture of the alkyl radical (V) by other than nitric oxide,³ and for the reaction of a peroxy radical with nitric oxide to give a nitrate.⁴

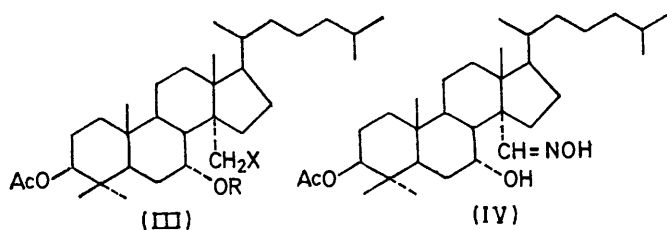
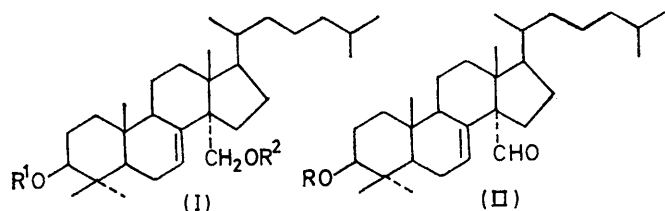
³ D. H. R. Barton, M. Akhtar, and P. G. Sammes, *J. Amer. Chem. Soc.*, 1965, **87**, 4601; D. H. R. Barton, D. Kumari, P. Welzel, L. J. Danks, and J. F. McGhie, *J. Chem. Soc. (C)*, 1969, 332.

⁴ J. R. Shelton and R. F. Kopczewski, *J. Org. Chem.*, 1967, **32**, 2908; E. G. Janzen, J. L. Meyer, and C. L. Ayers, *J. Phys. Chem.*, 1967, **71**, 3108; Y. Rees and G. H. Williams, *Adv. Free Radical Chem.*, 1969, **3**, 199.

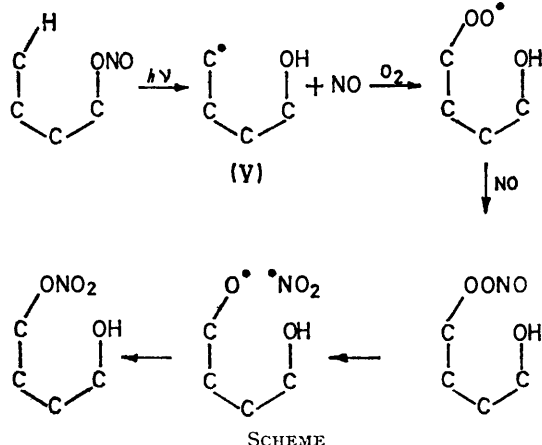
¹ P. L. Batten, T. J. Bentley, R. B. Boar, R. W. Draper, J. F. McGhie, and D. H. R. Barton, *J.C.S. Perkin I*, 1972, 739; T. J. Bentley, R. B. Boar, R. W. Draper, J. F. McGhie, and D. H. R. Barton, *ibid.*, p. 749.

² K. T. W. Alexander, M. Akhtar, R. B. Boar, J. F. McGhie, and D. H. R. Barton, *Chem. Comm.*, 1971, 1479; 1972, 383.

A previous report⁵ that photolysis of octyl nitrite in the presence of oxygen gives simply octyl nitrate has been modified by Chow and his co-workers⁶ who found that



similar photolysis of pentyl nitrite gave, amongst others, the rearranged products 4-hydroxy-1-methylbutyl nitrate (12.5%) and pentane-1,4-diyl dinitrate (9.5%). The latter workers have also demonstrated the formation of



rearranged nitrates in the photolysis of *N*-nitroso-amides in the presence of oxygen.⁷ Our results establish that the photo-oxidation of nitrites can be a synthetic method of some merit. For further transformations the nitrate group thus introduced has the advantage of being stable to both acidic and basic conditions whilst being readily convertible into the corresponding alcohol by mild reduction.

Treatment of the 7 α -hydroxy-32-nitrate (III; R = H, X = ONO₂) with methanesulphonyl chloride in pyridine afforded the 7 α -methylsulphonate-32-nitrate (III; R = SO₂Me, X = ONO₂) which without purification was stirred with basic alumina to give 3 β -acetoxy-5 α -lanost-7-en-32-yl nitrate (I; R¹ = Ac, R² = NO₂) in excellent

⁵ P. Kabasakalian and E. R. Townley, *J. Amer. Chem. Soc.*, 1962, **84**, 2711.

overall yield. Reduction of the nitrate group with zinc in acetic acid at room temperature then gave the desired 32-alcohol (I; R¹ = Ac, R² = H). Finally, oxidation with Jones reagent in acetone afforded the 32-aldehyde (II; R = Ac), identical with material prepared by the previous route.¹

EXPERIMENTAL

N.m.r. data, recorded at 60 MHz, refer to solutions in deuteriochloroform with tetramethylsilane as internal standard. Rotations are for solutions in chloroform. Column chromatography was on Merck silica gel 60.

3 β -Acetoxy-7 α -hydroxy-5 α -lanostan-32-yl Nitrate (III; R = H, X = ONO₂).—3 β -Acetoxy-5 α -lanostan-7 α -yl nitrite¹ (3 g) in dry benzene (500 ml) was irradiated using a 125 W high-pressure mercury vapour lamp with a Pyrex filter whilst a slow stream of dry oxygen was bubbled through the stirred solution. After 7 h (t.l.c. control) the solvent was evaporated off, and the residue chromatographed on silica (50 g). Elution with benzene-light petroleum (b.p. 40–60°) (60 : 40 v/v) afforded the nitrate (1.4 g, 44%), m.p. (from ethanol) 146–149° (decomp.), [α]_D +14° (c 0.14), ν_{\max} (Nujol) 3540 and 3480 (OH), 1720 and 1265 (OAc), and 1630, 1620, and 1280 (ONO₂) cm⁻¹, τ 5.08 and 5.45 (2H, ABq, *J* 10 Hz, 32-H₂), ca. 5.5 (1H, 3 α -H, obscured by 32-H₂ signal), and 5.96 (1H, m, 7 β -H) (Found: C, 70.05; H, 10.1; N, 2.5. C₃₂H₅₅NO₆ requires C, 69.9; H, 10.1; N, 2.55%).

3 β -Acetoxy-5 α -lanost-7-en-32-yl Nitrate (I; R¹ = Ac, R² = NO₂).—The above nitrate (1 g) in dry pyridine (30 ml) was treated with methanesulphonyl chloride (2 ml) at 0° for 24 h. The solution was poured into water and extracted with ether to give 3 β -acetoxy-32-nitrate-5 α -lanostan-7 α -yl methanesulphonate, ν_{\max} (CCl₄) 1735 and 1240 (OAc), 1633 and 1280 (ONO₂), and 1345 and 1175 (OSO₂Me) cm⁻¹. This material in benzene (100 ml) was stirred with Woelm basic alumina (20 g) for 12 h (t.l.c. control). The alumina was filtered off and washed thoroughly with ether. The combined filtrates were evaporated and the residue chromatographed on silica (50 g). Elution with benzene-light petroleum (b.p. 60–80°) (40 : 60 v/v) afforded 3 β -acetoxy-5 α -lanost-7-en-32-yl nitrate (830 mg, 86%), m.p. (from benzene-ethanol) 90–91°, [α]_D +46.4° (c 0.12), ν_{\max} (CCl₄) 1735 and 1240 (OAc), and 1635 and 1280 (ONO₂) cm⁻¹, τ 4.65 (1H, m, 7-H), 5.12 and 5.76 (2H, ABq, *J* 12 Hz, 32-H₂), and 5.45 (1H, m, 3 α -H) (Found: C, 72.5; H, 10.0; N, 2.55. C₃₂H₅₃NO₅ requires C, 72.3; H, 10.05; N, 2.6%).

3 β -Acetoxy-5 α -lanost-7-en-32-ol (I; R¹ = Ac, R² = H).—3 β -Acetoxy-5 α -lanost-7-en-32-yl nitrate (300 mg) in glacial acetic acid (50 ml) was stirred at room temperature for 3.5 h with activated zinc dust (5 g). The mixture was filtered through Celite and the filter cake washed thoroughly with ether. The total filtrate was poured into water and extracted with ether. The extracts were washed with 1*N*-sodium carbonate solution, then water, dried, and evaporated. Crystallisation of the residue from methanol gave 3 β -acetoxy-5 α -lanost-7-en-32-ol (230 mg, 84%), m.p. 152–

⁶ Y. L. Chow, T. Hayasaka, and J. N. S. Tam, *Canad. J. Chem.*, 1970, **48**, 508. See also A. Mackor and Th. J. De Boer, *Rec. Trav. chim.*, 1970, **89**, 164; H. Sugimoto, T. Kojima, K. Orito, and T. Masamune, *Tetrahedron*, 1971, **27**, 291; H. A. Wiebe, A. Villa, T. M. Hellman, and J. Hecklen, *J. Amer. Chem. Soc.*, 1973, **95**, 7; C. W. Spicer, A. Villa, H. A. Wiebe, and J. Hecklen, *ibid.*, p. 13.

⁷ Y. L. Chow and J. N. S. Tam, *Chem. Comm.*, 1969, **747**.

153°, $[\alpha]_D + 32.5^\circ$ (c 0.28), $\nu_{\max.}$ (CCl₄) 3530 (OH) and 1735 and 1240 (OAc) cm^{-1} , τ 4.63 (1H, m, 7-H), 5.50 (1H, m, 3 α -H), and 6.36 and 6.76 (2H, ABq, J 10 Hz, 32-H₂) (Found: C, 78.9; H, 11.0. C₃₂H₅₄O₃ requires C, 79.0; H, 11.2%).

3 β -Acetoxy-5 α -lanost-7-en-32-al (II; R = Ac).—3 β -Acetoxy-5 α -lanost-7-en-32-ol (100 mg) in AnalaR acetone (40 ml) was cooled to -30° and Jones chromium trioxide reagent (3 drops) added. After 1 h the solution was allowed to warm to room temperature and after a further 5 min the mixture was poured into water containing 10% methanol. Extrac-

tion with ether gave the 32-aldehyde (90 mg, 90%), m.p. (from methanol) 130—131°, $[\alpha]_D + 27.5^\circ$ (c 0.13) {lit., m.p. 144—145° (sealed tube), $[\alpha]_D + 24^\circ$ }, $\nu_{\max.}$ (Nujol) 1730 and 1250 (OAc) and 1712 (CHO) cm^{-1} , τ 0.38 (1H, s, CHO), 4.6 (1H, m, 7-H), and 5.5 (1H, m, 3 α -H), identical with an authentic sample.

We thank Chelsea College for a research studentship (to J. A.).

[3/1137 Received, 4th June, 1973]